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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,337	09/18/2000	Takuya Tamatani	SHIM-006	8342

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,337	TAMATANI ET AL.	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/18/01; 12/4/01* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *104-108,121,123,127-144 and 155* is/are pending in the application.

4a) Of the above claim(s) *136-141, 143 and 144* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *104-108,121,123,127-135,142 and 155* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 September 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 104-108, 121, 123, 127-144 and 155 are pending.

2. Applicant's election with traverse of Group IX, Claims 104-106, 121, 123, 125-135 and 142, drawn to monoclonal antibody produced by Hydridoma FERM BP-6208, filed 12/4/01, is acknowledged. The traversal is on the grounds that (1) applicant has amended claim 104 to direct to a non-human monoclonal antibody or portion thereof which is reactive to human, mouse and rat connective tissue growth factors, (2) Applicants recognize that by combining Groups IX, X and XIX, any art cited against the claims of Groups IX drawn to hybridoma FERM BP-6208 may also be citable against claims of Group X, drawn to hybridoma FERM BP-6209 or claims of Group XIX drawn to a method for detecting CTGF using antibodies produced by hybridoma FERM BP-6208 or hybridoma FERM BP-6209. Upon reconsideration and in response to applicant's election with traverse to the restriction requirement, the restriction of Groups X has been rejoined with Group IX. Therefore, the requirement of Group IX (now claims 104-108, 121, 123, 127-135, 142 and 155) and Groups I-VIII, XI-XXIII is still deemed proper and is therefore made FINAL.

3. Claims 136-141, 143 and 144 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 104-108, 121, 123, 127-135, 142 and 155 are being acted upon in this Office Action.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 104-108, 121, 123, 127-135, 142 and 155 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the hybridomas FERM BP-6208 and BP-6209 in claims 105-108 and 127 and kidney-derived fibroblast cell line 293-T (ATCC CRL 1573) recited in claim 155 are required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the hybridomas, which produce these antibodies, may satisfy first paragraph. See 37 CFR 1.801-1.809.

It is noted that hybridomas FERM BP-6208 and BP-6209 have been deposited as indicated on page 75 of the specification. However, it is not apparent if the deposit has been made under the terms of the Budapest Treaty.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridomas FERM BP-6208 and BP-6209 have been deposited under the Budapest Treaty and that the hybridomas will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or **for the enforceable life of the patent whichever is longer**. See 37 CFR 1.806.

If the deposit has not been made under the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

It is noted that kidney-derived fibroblast cell line 293-T (ATCC CRL 1573) is commercially available from ATCC as indicated on page 83 of the specification. The Office will accept commercial availability as evidence that a biological material is known and readily available only when the evidence is clear and convincing that the public has access to the material. See the final rule entitled "Deposit of Biological Materials for Patent Purposes," 54 FR 34864, 34875 (August 22, 1989). A product could be commercially available but only at a price that effectively eliminates accessibility to those desiring to obtain a sample.

The specification does not reasonably provide enablement for (1) *any* non-human monoclonal antibody or portion thereof which is reactive to human, mouse and rat connective tissue growth factors (CTGFs) as recited in claim 104, (2) *any* non-human monoclonal antibody or portion thereof comprises *any* property substantially equivalent to that of a monoclonal antibody produced by a hybridoma identified by international deposit accession No. FERM BP-6208 as recited in claim 106, (3) *any* non-human monoclonal antibody or portion thereof comprises *any* property substantially equivalent to that of a monoclonal antibody produced by a hybridoma identified by international deposit accession No. FERM BP-6209 as recited in claim 108, (4) *any* cell producing *any* non-human monoclonal antibody as recited in claim 121, (4) *any* hybridoma obtainable by fusing a mammalian myeloma cell with a mammalian B cell which is capable of producing any non-human monoclonal antibody as recited in claim 123, (5) *any* antibody-immobilized insoluble carrier as recited in claim 128, (6) *any* non-human antibody-immobilized insoluble carrier wherein said carrier is selected from the group consisting of plates, test tubes, tubes, beads, balls, filters, and membrane as recited in claim 129, (7) *any* non-human antibody-immobilized insoluble carrier wherein said carrier is a filter or membrane, or that used for affinity column chromatography as recited in claim 130, (8) *any* labeled antibody which is prepared by labeling *any* non-human monoclonal antibody or a portion thereof with a labeling agent capable of providing a detectable signal by itself or together with any other substances as recited in claim 131, (9) *any* labeled non-human antibody wherein said labeling agent is an enzyme, fluorescent substance, chemiluminescent substance, biotin, avidin, or radioisotope as recited in claim 132, (10) a kit for detecting or assaying any mammalian CTGF comprising *any* non-human monoclonal antibody or portion thereof as recited in claim 133, (11) a kit for detecting or assaying any mammalian CTGF comprising *any* antibody-immobilized insoluble carrier on which the said non-human monoclonal antibody is immobilized as recited in claim 134, (12) a kit for detecting or assaying *any* mammalian CTGF comprising a labeled antibody which is prepared by labeling *any* non-human monoclonal antibody or a portion thereof with a labeling agent capable of providing a detectable signal by itself or together with *any* other substances as recited in claim 135, (13) a kit for separating or purifying *any* mammalian CTGF comprising *any* antibody-immobilized insoluble carrier on which *any* non-human monoclonal antibody is immobilized as recited in claim 142 and (14) *any* non-human monoclonal antibody or a portion thereof characterized by inhibiting the binding of human CTGF to human kidney-derived fibroblast cell line 293-T (ATCC CRL1573) for detection assays as recited in claim 155.

The specification discloses only (1) a mouse anti-human CTGF monoclonal antibody produced by hybridoma BP-6208 (clone 8-86-2) that cross-reacts with human, mouse and rat connective tissue growth factor (CTGF) (See page 99, lines 15-16, Fig 1) and (2) a mouse anti-human CTGF monoclonal antibody that produced by hybridoma BP-6209 (clone 8-64-6) that cross-reacts with human and mouse CTGF (See page 98, lines 30-34, Fig 1). Both antibodies inhibit the binding of human CTGF to human 293 fibroblast (Fig 1 and Fig 5-7) for detection assays such as ELISA (See page 99-102, Fig 21). The specification discloses additional antibodies such as the ones listed in Figs 1 & 2. However, not every antibody listed in Fig 1&2 has the same properties as the claimed antibodies produced by hybridoma BP-6208 and hybridoma BP-6209. The specification discloses only a full-length rat CTGF polypeptide consisting of SEQ ID NO: 2 and human CTGF polypeptides consisting of SEQ ID NOS: 5-16, 18, 20, 22 and 24. The specification does not provide any guidance as how to make and use *any* antibody that binds to *any* mammalian CTGF other than the specific CTGF mentioned above. There is insufficient information regarding to the epitope (specific amino acid residues) to which the antibody binds and whether the binding specificity is sequential or conformational dependent.

Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide. Given the indefinite number of undisclosed antibody encompassed by the claims, it is unpredictable which undisclosed antibody would bind to just any mammalian CTGFs and would have the same functional characteristics as monoclonal antibody produced by hybridoma BP-6208 and hybridoma BP-6209 such as inhibiting the binding of human CTGF to 293 fibroblast. It follows that *any* cell or hybridoma producing *any* undisclosed non-human monoclonal antibody is not enable. It also follows that *any* labeled undisclosed non-human monoclonal antibody or portion thereof and kit comprising *any* undisclosed non-human monoclonal antibody are not enabled.

For these reasons, the specification as filed fails to enable one skill in the art to practice the invention without undue amount of experimentation. As such, further research would be required to practice the claimed invention.

7. Claims 104, 106, 108, 121, 123, 128-135, 142 and 155 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses only (1) a mouse anti-human CTGF monoclonal antibody produced by hybridoma BP-6208 (clone 8-86-2) that cross-reacts with human, mouse and rat connective tissue growth factor (CTGF) (See page 99, lines 15-16, Fig 1) and (2) a mouse anti-human CTGF monoclonal antibody that produced by hybridoma BP-6209 (clone 8-64-6) that cross-reacts with human and mouse CTGF (See page 98, lines 30-34, Fig 1). Both antibodies inhibit the binding of human CTGF to human 293 fibroblast (Fig 1 and Fig 5-7) for detection assays such as ELISA (See page 99-102, Fig 21).

The specification does not reasonably provide a **written description** of (1) *any* non-human monoclonal antibody or portion thereof which is reactive to human, mouse and rat connective tissue growth factors (CTGFs), (2) *any* non-human monoclonal antibody or portion thereof comprises *any* property substantially equivalent to that of a monoclonal antibody produced by a hybridoma identified by international deposit accession No. FERM BP-6208, (3) *any* non-human monoclonal antibody or portion thereof comprises *any* property substantially equivalent to that of a monoclonal antibody produced by a hybridoma identified by international deposit accession No. FERM BP-6209, (4) *any* cell producing *any* non-human monoclonal antibody, (4) *any* hybridoma obtainable by fusing a mammalian myeloma cell with a mammalian B cell which is capable of producing any non-human monoclonal antibody, (5) *any* antibody-immobilized insoluble carrier, (6) *any* non-human antibody-immobilized insoluble carrier wherein said carrier is selected from the group consisting of plates, test tubes, tubes, beads, balls, filters, and membrane, (7) *any* non-human antibody-immobilized insoluble carrier wherein said carrier is a filter or membrane, or that used for affinity column chromatography, (8) *any* labeled antibody which is prepared by labeling *any* non-human monoclonal antibody or a portion thereof with a labeling agent capable of providing a detectable signal by itself or together with any other substances, (9) *any* labeled non-human antibody wherein said labeling agent is an enzyme, fluorescent substance, chemiluminescent substance, biotin, avidin, or radioisotope, (10) a kit for detecting or assaying any mammalian CTGF comprising *any* non-human monoclonal antibody or portion thereof, (11) a kit for detecting or assaying any mammalian CTGF comprising *any* antibody-immobilized insoluble carrier on which the said non-human monoclonal antibody is

immobilized, (12) a kit for detecting or assaying *any* mammalian CTGF comprising a labeled antibody which is prepared by labeling *any* non-human monoclonal antibody or a portion thereof with a labeling agent capable of providing a detectable signal by itself or together with *any* other substances (13) a kit for separating or purifying *any* mammalian CTGF comprising *any* antibody-immobilized insoluble carrier on which *any* non-human monoclonal antibody is immobilized and (14) *any* non-human monoclonal antibody or a portion thereof characterized by inhibiting the binding of human CTGF to human kidney-derived fibroblast cell line 293-T (ATCC CRL1573) for detection assays.

With the exception of monoclonal antibodies that produced by the hybridomas mentioned above, there is no description about the structure associated with function of *any* connective tissue growth factors (CTGFs) to which the antibody binds. Further, the specification fails to describe additional representative species of non-human monoclonal antibody that binds to just about *any* CTGFs. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Given the lack of description and the lack of additional representative species as encompassed by the claim, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.* Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 106, 108, 131 and 135 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "a property substantially equivalent to" as recited in claims 106 and 108 is indefinite and ambiguous. A person of ordinary skill in the art cannot appraise the metes and bounds of the term "a property substantially equivalent".

The recitation of "with other substances" as recited in claims 131 and 135 is indefinite and ambiguous. A person of ordinary skill in the art cannot appraise the metes and bounds of the term "other substances" since the specification does not define "other substances".

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 104, 106, 108 and 155, are rejected under 35 U.S.C. 102(b) as being anticipated by US Pat 5,408,040 (April 1995, PTO 1449).

The '040 patent teaches a monoclonal antibody or the binding portion thereof made in the mouse which is non-human that binds to the human connective tissue growth factor (CTGF) (See Abstract, column 7, lines 40-62, claims 2 and 4 of '040, in particular). The reference antibody is substantially equivalent to that of the claimed monoclonal antibody since the reference antibody binds to human CTGF and inherently would cross-reacts with mouse CTGF and perhaps rat CTGF given that the immunogen used to generate the reference antibody is a full-length human connective tissue factor wherein the amino acid sequence has a large region identical to mouse and rat. The recitation of "substantially equivalent" in claims 106 and 108 expands the claimed antibody to read on the prior art antibody. While the reference is silent that the reference antibody has the property of that recited in claim 155 where the antibody inhibits the binding of human CTGF to human kidney-derived fibroblast cell line 293-T (ATCC CRL1573), the functional properties are the inherent property of the reference antibody. Therefore the claimed antibody appears to be the same as the prior art antibody. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

12. Claims 104, 106, 108, 121, 123, 128-132 and 155 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat 5,783,187 (July 1998, PTO 1449).

The '187 patent teaches a mouse monoclonal antibody which is non-human or the binding fragment thereof made in the mouse and screening hybridoma that binds to the human connective tissue growth factor (CTGF) (See Abstract, column 5, lines 19-33, in particular). The reference antibody is substantially equivalent to that of the claimed monoclonal antibody since the reference antibody binds to human CTGF and inherently would cross-reacts with mouse CTGF and perhaps rat CTGF given that the immunogen used to generate the reference antibody is a full-length human connective tissue factor wherein the amino acid sequence has a large region identical to mouse and rat. The recitation of "substantially equivalent" in claims 106 and 108 expands the claimed antibody to read on the prior art antibody. Claim 121 is included in this rejection because monoclonal antibody is produced by hybridoma, which is a cell that produces the reference antibody. The '187 patent teaches a method of detecting the level of CEGF using the reference anti-CEGF antibody in radioimmunoassay, ELISA and immunofluorescence wherein these assays require the reference antibodies to immobilized to an insoluble carrier such as plate for ELISA, test tube or tubes for radioimmunoassay (See column 6, lines 10-21, in particular). The '187 patent further teaches antibody affinity column chromatograph (See column 7, lines 48-60, column 8, lines 35-38, in particular). Claims 131 and 132 are included in this rejection because the '187 teaches immunofluorescence ELISA wherein the reference antibody is either labeled with a fluorescent substance or together with other substance such as indirect ELISA wherein the secondary antibody is labeled.

While the reference is silent that the reference antibody has the property of that recited in claim 155 where the antibody inhibits the binding of human CTGF to human kidney-derived fibroblast cell line 293-T (ATCC CRL1573), the functional properties are the inherent property of the reference antibody. Therefore the claimed antibody appears to be the same as the prior art antibody. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 121 and 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat 5,408,040 (April 1995, PTO 1449) in view of Harlow *et al* (in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, pages 139-149).

The teachings of the '040 patent have been discussed supra.

The claimed invention recited in claim 121 differs from the reference only by the recitation of a cell producing the non-human monoclonal antibody which reactive to human, mouse, and rat connective tissue growth factors (CTGFs).

The claimed invention recited in claim 123 differs from the reference only by the recitation of the cell is a hybridoma obtainable by fusing a mammalian myeloma cell with a mammalian B cell which is capable of producing the non-human monoclonal antibody.

Harlow *et al* teach a method of producing monoclonal antibody by fusing any mammalian B cell to a mammalian myeloma cell, the immortalized antibody producing cell or hybridoma is capable of producing monoclonal antibody in unlimited quantities (See page 139-149, in particular). Harlow *et al* further teach monoclonal antibodies produced by hybridoma are useful because of their specificity of binding, their homogeneity and their ability to be produced by cell or hybridoma in unlimited quantities (See page 141, last full paragraph, in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make hybridoma which is cell that produce monoclonal antibody

in unlimited quantities as taught by Harlow *et al* with the human connective tissue growth factor as taught by the '040 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to make do this because Harlow *et al* teach that hybridoma or cell can produce monoclonal antibody in unlimited quantities (See page 141, last full paragraph, in particular).

16. Claims 131-135 and 142 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat 5,408,040 (April 1995, PTO 1449) or US Pat 5,783,187 (July 1998, PTO 1449) each in view of U.S. Pat No. 6,107,049 (filed Dec 8, 1997, PTO 892; see entire document).

The teachings of the '040 and '187 patents have been discussed supra.

The claimed invention recited in claim 131 differs from the references only by the recitation of a labeled antibody.

The claimed invention recited in claim 132 differs from the references only by the recitation of a labeled antibody wherein the labeling agent is an enzyme, fluorescent substance, chemiluminescent substance, biotin, avidin or radioisotope.

The claimed invention recited in claim 133 differs from the references only by the recitation of a kit for detecting or assaying mammalian CEGF comprising non-human monoclonal antibody or a portion thereof.

The claimed invention recited in claim 134 differs from the references only by the recitation of a kit for detecting or assaying mammalian CEGF comprising an antibody immunobilized carrier on which the non-human monoclonal antibody is immobilized.

The claimed invention recited in claim 135 differs from the references only by the recitation of a kit for detecting or assaying mammalian CEGF comprising a labeled antibody.

The claimed invention recited in claim 142 differs from the references only by the recitation of a kit for separating or purifying mammalian CEGF comprising an antibody immobilized carrier on which the non-human monoclonal antibody is immobilized.

The '049 patent teaches a kit comprising an antibody specific for cPSA for diagnostic assays, separation and detection assays (See column 11, line 44-57, claims 12-17 of '049, in particular). The '049 patent teaches the reference antibody is immobilized on a solid carrier such as a plate, magnetic particle which are beads wherein the antibody is fluorescein labeled or

enzymatically labeled such as alkaline phosphatase (See column 11, lines 46-49, claims 18-20 of '049, in particular). The '049 patent further teaches the method of detection is conveniently provided in the form of a kit that is a packaged collection of reagents or combination of other assay components as necessary and appropriate for the needs of the user (See column 9, lines 46-51, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the CTGF antibody as taught by the '040 patent or the CTGF antibody as taught by the '187 patent for the a kit comprising CTGF antibody either labeled or not labeled for diagnostic assays as taught by the '049 patent. One would have been motivated, with a reasonable expectation of success, to place the antibody taught by the '049 in a kit affixed to a 96-well plate (solid phase) for convenience and commercial expedience. A kit will allow for ease of use for the practitioner since all the necessary reagents, standard and instructions for use are included in a kit as taught by '049 (See column 9, lines 46-51, in particular). From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidence by the references.

17. Claims 105, 107 and 127 are free of prior art.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

20. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
January 28, 2002

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP ~~1800~~ 1640